

## **Clinical and immunologic effects of aglatimagene besadenovec combined with radiotherapy in intermediate-risk localized prostate cancer: integrated results from the PRTK03 and PRTK05 clinical trials**

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### **Abstract**

#### **Background:**

Intermediate-risk prostate cancer (PCa) is the largest localized disease group treated with curative-intent external beam radiation (EBRT)+/- androgen deprivation therapy (ADT) (~65,000 US patients annually). Aglatimagene besadenovec synergizes with curative-intent EBRT by inducing immunogenic tumor-cell death and promoting antitumor immunity.

We analyzed biomarker data from PrTK03, a randomized, placebo-controlled phase 3 clinical trial, and PrTK05, a randomized phase 2 trial, to characterize the extent of local and systemic immune activation following aglatimagene treatment in patients with intermediate-risk PCa.a.

#### **Methods:**

Of 745 patients randomized in PrTK03, 635 (85%) had intermediate-risk PCa and received aglatimagene plus EBRT±ADT (422) or placebo plus EBRT±ADT (213). Efficacy analyses included disease-free survival (DFS), time to biochemical failure (TTBF), time to metastasis (TTM), and time to new anticancer therapy (TTNT). Centrally reviewed biopsies obtained 2 years after radiation assessed pathological response; AI-enabled H&E analysis evaluated lymphocytic infiltration and spatial lymphocyte–tumor interactions.

PrTK05 enrolled 25 intermediate-risk patients treated with aglatimagene plus EBRT±ADT and 7 treated with SOC. Serial blood samples were analyzed by multiparameter flow cytometry to characterize systemic immune changes following treatment.

#### **Results:**

PrTK03 met its primary endpoint, with a 30% reduction in DFS risk versus control (HR 0.70; 95% CI 0.52–0.94; p=0.0155). With follow-up through March 15, 2026 (median, 58.0 months), the intermediate-risk population showed a 41% reduction in PCa recurrence or PCa-specific death (HR 0.59; 95% CI 0.41–0.84; p=0.0034). Favorable effects were also observed for TTBF (HR 0.48; 95% CI 0.22–1.03), TTNT (HR 0.51; 95% CI 0.24–1.10), and TTM (HR 0.10; 95% CI 0.01–0.85). Among 277 patients with centrally reviewed biopsies obtained 22–26 months after treatment, negative biopsies occurred in 76.6% (144/188) with aglatimagene versus 60.7% (54/89) with control; positive biopsies occurred in 20.7% versus 38.2%, respectively (stratified CMH p=0.0034; chi-square p=0.0026).

Exploratory digital pathology showed increased lymphocytic infiltration after treatment in both arms (p<0.001). In paired biopsies with detectable post-treatment tumor (n=98), aglatimagene increased intratumoral lymphocyte fraction (p=0.011), lymphocyte–tumor neighbor and mixing scores (both p<0.001) and reduced the median tumor-to-lymphocyte distance versus control (p=0.027).

Preliminary PrTK05 flow-cytometry analyses indicate expansion of circulating CD8<sup>+</sup> effector and effector-memory T cells, including proliferating Ki67<sup>+</sup> and cytotoxic GZMB<sup>+</sup>Ki67<sup>+</sup> CD8<sup>+</sup> subsets associated with aglatimagene treatment. Comparison with SOC is ongoing.

**Conclusions:**

Aglatimagene plus EBRT improved DFS and reduced metastatic progression in intermediate-risk localized PCa. In post-treatment biopsies obtained more than 2 years after treatment, aglatimagene was associated with greater pathological tumor clearance and durable remodeling of the PCa tumor microenvironment, characterized by increased and closer lymphocyte–tumor interactions. Complementary peripheral immune findings demonstrate expansion and activation of cytotoxic CD8<sup>+</sup> T-cell populations, supporting a mechanism of sustained anti-tumor immune surveillance beyond local disease control.

**Funding Acknowledgements:**

The study was funded by Candel Therapeutics

**Conflicts of Interest Disclosure Statement:**

F. Barone, A. Manzanera, S. Rao, A. Cruz, J. Dwyer, S. Kammerman, Q. Guo, M. A.R. Diers, J. Buie, J. Makin, G. Nichols, P.P. Tak are employees of Candel Therapeutics.

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